

# Outcome of Graves' disease

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs Universitet kommer att offentligens försvaras i sal Arvid Carlsson, Medicinaregatan 3, Göteborg, den 21:a februari 2020, klockan 09.00

av Mats Holmberg

Fakultetsopponent:

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## Avhandlingen baseras på följande delarbeten

I. Sjölin G\*, **Holmberg M\***, Törring O, Byström K, Khamisi S, de Laval D, Abraham-Nordling M, Calissendorff J, Lantz M, Hallengren B, Filipsson Nyström H, Wallin G. The long-term outcome of treatment for Graves' hyperthyroidism. Published in Thyroid 2019; nov 29(11):1545-1557.

\*Gabriel Sjölin and M Holmberg have contributed equally

II. **Holmberg M**, Malmgren H, Berglund PF, Johansson B, Klasson N, Skau S, Filipsson Nyström H. Predictors for mental symptoms in Graves' disease. Manuscript

III. **Holmberg M**, Malmgren H, Berglund PF, Heckemann RA, Johansson B, Klasson N, Olsson E, Skau S, Starck G, Filipsson Nyström H. A longitudinal study of medial temporal lobe volumes in Graves' disease. Manuscript

**SAHLGRENKA AKADEMIN  
INSTITUTIONEN FÖR MEDICIN**



# Outcome of Graves' disease

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## Abstract

Graves' disease (GD) is an autoimmune condition with symptoms suggesting an affected brain. The overall aim of this thesis is to characterize the consequences of GD with a special focus on the brain.

**Paper I** was a longitudinal cohort study that assessed long-term treatment results 6–10 years after the onset of GD. Patients, initially treated with antithyroid drugs had a 40% chance of being euthyroid without thyroid medication at follow-up. One in four patients did not feel fully recovered.

**Paper II** was a longitudinal case-control study designed to characterize affective and cognitive symptoms in women with untreated GD. At onset of GD, the patients were significantly more affected with depression, anxiety, and mental fatigue compared to controls. At follow-up after 15 months, these symptoms remained in a significant proportion of patients. Patients with eye symptoms or a history of psychiatric conditions were more likely to be affected with brain-related symptoms.

**Paper III** was a longitudinal case-control study of women with untreated GD designed to investigate the effect of GD on hippocampal volumes. At onset of GD, hippocampus and amygdala volumes of the patients were smaller compared to controls. After 15 months, only the left amygdala remained smaller than in controls. At inclusion, there was an inverse correlation between thyroid-stimulating hormone receptor antibody (TRAb) and the volumes of both amygdalae and the right hippocampus. There were also inverse correlations between TRAb and free triiodothyronine recovery and the recovery of most of the four assessed brain volumes.

In summary, the studies demonstrate that Graves' hyperthyroidism has unexpected long-term consequences for many patients, provide extensive new data on the serious and chronic nature of GD, and show for the first time that GD is accompanied by reversible brain changes.

**Keywords:** Graves' disease, Quality of life, Depression, Anxiety, Magnetic resonance imaging, Mental fatigue, Volumetry, Hippocampus, Amygdala